REMARKS

Claims 1, 2 and 4-12 are now in the application. Claims 1 and 2 have been amended to recite "an effective amount" and claims 4-6 have been amended to recite "adenosine and inorganic phosphate" in place of "adenosine".

Claim 13 was objected to under 37 CFR 1.75(c). Claim 13 is now canceled.

Claims 4-6 were rejected under 35 U.S.C. 112, second paragraph. Claims 4-6 were amended to recite adenosine and inorganic phosphate in line with claims 1 and 2 as was requested in the Office Action.

The objection to claim 13 and rejections of claim 13 under 35 U.S.C. 112, second paragraph and under 35 U.S.C. 112, first paragraph have been rendered moot by its cancellation.

Claims 1-2, 7, 9-10 and 12-13 were rejected under 35 U.S.C. 102(b) as being anticipated by Friedlander (U.S. Patent No. 5,055,460) as evidenced by Lehninger (Biochemistry, Worth Publishers, Inc., New York, 1970, pages 289-290). Claims 1-2 and 7-13 were rejected under 35 U.S.C. 102(b) as being anticipated by Astrup (U.S. Patent No. 5,422,352) as evidenced by Lehninger. Claims 1-2, 7, 10, 12 and 13 were rejected under 35 U.S.C. 102(b) as being anticipated by Allen (U.S. Patent No. 5,480,657) as evidenced by Lehninger. The cited references do not anticipate claims 1-2 and 7-12 as now amended. The three U.S. patents cited disclose that, 1. caffeine, aspirin and ephedrine may be administered concurrently with caloric restriction or with a commercial diet program for the purpose of reducing weight or maintaining body weight (Friedlander), 2. caffeine and ephedrine may be administered along with food for the purpose of reducing the weight of a human (Astrup) and 3. caffeine, fructose and chromium, may be consumed with meals for the purpose of reducing weight or maintaining body weight (Allen). The Office Action argues that "claims 1-2 and 7-13 encompass 'administration' of any amount of AMP or ATP. This includes a single molecule of such compounds. As such, any normal diet wherein cellular matter is consumed reasonably reads on the claims because all cells have AMP and ATP in them." (page 2 of office action). Furthermore, "Lehninger teaches that ATP, ADP, and AMP" "...are not trace substances; the sum of their concentration in the aqueous phase of various types of intact cells is between 2 and 15 mM" and "Lehninger teaches that very little ATP exists as a free anion, rather, it is largely present as a 1:1 $MgATP^{2+}$ complex" (page 6

of the Office Action). "Accordingly, it is the Office Action's position that the consumption of a normal diet or a commercial diet plan will naturally result in the consumption of at least one molecule of AMP or ATP because these substances are present in all cells, including the cells of beef products, fish products, chicken products, vegetables, etc." (page 7 of the Office Action).

Claims 1 and 2 have been amended to recite "an effective amount of: (a) adenosine and inorganic phosphate; (b) adenosine 5'-monophosphate; and (c) adenosine 5'-triphosphate."

Regarding the references by Friedlander, Astrup and Allen, which are argued to have anticipated the present claims, these three patents claim ephedrine (Friedlander and Astrup) or chromium (Allen) as being administered along with caffeine as part of a weight loss or weight maintenance program. These three patents do not anticipate the present claims because they do not teach administration of an adenosine compound, let alone administration of an effective amount of an adenosine compound. It is important to note that Friedlander and Astrup require ephedrine along with caffeine. Ephedrine is a dangerous chemical, which is an analogue of amphetamine acting by binding to adrenergic receptors and therefore stimulating bodily metabolism. Ephedrine was used effectively in the past for weight loss purposes. Ephedrine was used for weight loss purposes as a single agent and because of its established thermogenic and appetite suppressant activity was known to be effective without the presence of caffeine. The use of ephedrine is now prohibited by the FDA. On February 6, 2004, the FDA issued the following regulation:

"The Food and Drug Administration (FDA) today issued a final rule prohibiting the sale of dietary supplements containing ephedrine alkaloids (ephedra) because such supplements present an unreasonable risk of illness or injury. The rule will become effective 60 days from the date of publication."

"This FDA rule reflects what the scientific evidence shows - that ephedra poses an unreasonable risk to those who use it," Health and Human Services Tommy G. Thompson said. "The regulations prohibit the sale of dietary supplements containing ephedra, and we intend to take swift action against anyone who puts consumers at risk by continuing to sell such products after the prohibition takes effect."

The use of chromium with caffeine (Allen) can not advance any argument related to caffeine alone, since chromium compounds by themselves were used as weight loss promoting agents.

The following is an abstract copied from Medline, analyzing human trials which utilized chromium in weight loss.

Int. J. Obes. Relat. Metab. Disord. 2003 Apr; 27(4):522-9.
Chromium picolinate for reducing body weight: meta-analysis of randomized trials.
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The aim of this meta-analysis was to assess the evidence of chromium picolinate for reducing body weight. Literature searches were conducted on Medline, Embase, The Cochrane Library, Amed and Ciscom. Nine experts and four manufacturers of commercial preparations containing chromium picolinate were asked to contribute published and unpublished studies. There were no restrictions regarding the language of publication. The screening of studies, selection, data extraction, validation and the assessment of methodological quality were performed independently by two reviewers. To be included, studies were required to state that they were randomized, double-blind and placebo-controlled, and report on body weight. Ten trials met all inclusion criteria and provided data, which were suitable for statistical pooling. For body weight a significant differential effect was found in favour of chromium picolinate (weighted mean difference: -1.1 kg; 95% confidence interval (CI): -1.8 to -0.4 kg, n=489). Sensitivity analysis suggests that this effect is largely dependent on the results of a single trial (weighted mean difference: -0.9 kg; 95% CI: -2.0 to 0.2 kg, n=335). Three of the reviewed trials reported on adverse events, indicating their absence in the treatment groups. In conclusion, our meta-analysis suggests a relatively small effect of chromium picolinate compared with placebo for reducing body weight. The clinical relevance of the effect is debatable and the lack of robustness means that the result has to be interpreted with caution.

PMID: 12664086 [PubMed - indexed for MEDLINE]

Lehninger, according to the Office Action, supports the argument that food contains residual levels of adenosine and inorganic phosphate, AMP and ATP.

Since Lehninger refers to intact ("living") cells and food is comprised of dead cells, most of the ATP, AMP and adenosine and inorganic phosphate in food is degraded by catabolic enzymatic activities. Applicant concedes that consumed food contains more than one molecule of ATP, AMP and adenosine and inorganic phosphate in a form bound to fiber, membrane, protein or other cellular material. Food, however, in addition to undefined mixtures or forms (absorbed, bound or free) of ATP, AMP and adenosine and inorganic phosphate, contains inorganic ions and salts, mixtures of thousands of metabolites, which are small molecules, tens of thousands of fragmented proteins and peptides, tens of thousands of fragmented DNA pieces and oligodeoxyribonucleotides and tens of thousands of fragmented RNA pieces and oligoribonucleotides of different sequences shapes and forms. The claims of the present application recite administration of an effective amount of a member selected from a group consisting of (a) adenosine and inorganic phosphate; (b) AMP (adenosine 5'-monophosphate); and (c) ATP (adenosine 5'-triphosphate) in combination with caffeine or theophylline. In other words, a maximum of two, well- defined active agents rather than totally undefined mixtures of all of the active agents along with thousands of metabolites and tens of thousands of other molecules and fragments of high molecular weight proteins and nucleic acids of various structures, monomers, oligomers or polymers, which are constituents of food.

More importantly, applicant maintains that the references cited in the Office Action as evidenced by Lehninger, rather then anticipate the present application, **teach away** from it. The mechanism of ATP, AMP or adenosine and inorganic phosphate absorption and their incorporation into liver ATP pools is established and is described in the present application (column 6, line 26- column 6, line 43) "After the release of the therapeutic composition of ATP in the small intestine, absorption of adenosine and inorganic phosphate-the catabolic products of ATP, or of ATP itself then follows. Absorption of ATP itself is followed by a rapid degradation to adenosine and inorganic phosphate inside the vascular bed (Slakey et al. 1990; Rapaport and Fontaine 1989; Rapaport and Fontaine 1989b). Both the adenosine and inorganic phosphate are then incorporated into the liver ATP pools (steady state levels), effectively expanding-these pools (Rapaport and Zamecnik 1976; Rapaport and Fontaine 1989). The turnover of the expanded liver ATP pools, ATP pools which supply the adenosine precursor for red blood cell ATP synthesis, then lead to the expansion of red blood cell ATP pools. Expanded red blood cell

ATP pools are in turn released from red blood cells into the blood plasma compartment (extracellular) via a non-hemolytic mechanism, where they are rapidly degraded to adenosine and inorganic phosphate (Slakey et al. 1990; Rapaport and Fontaine 1989; Rapaport 1990)."

The Office Action's argument is flawed because food contains not only small amounts of adenosine and inorganic phosphate and AMP and ATP, but also the precursors of bodily energy, namely fats, sugars and proteins. In obesity or overweight, food is metabolized mostly to fats with minute amounts of fuel converted to energy (ATP), whereas in healthy non-obese individuals most of the food is metabolized to energy. Enclosed is a publication, Wlodek D and Gonzales M: Decreased energy levels can cause and sustain obesity. Journal of Theoretical Biology 2003, 225:33-44. Figure 1 on page 34 illustrates the distribution of food fuel between fat and energy in healthy and obese people. In obesity, although food may directly contribute minute amounts of adenosine and inorganic phosphate and AMP and ATP to liver ATP pools, which are the precursors of elevated blood plasma adenosine, the fuel (caloric) portion of the food will not contribute to liver ATP pools but to accumulation of fats. Therefore, in obese or overweight individuals, food, although containing minute amounts of adenosine and inorganic phosphate and AMP and ATP, would act mostly in increasing fat storage, rather than generating adenosine levels that will be sufficient to desensitize adipose tissue adenosine A1 receptors for producing net lipolysis. The administration of adenosine and inorganic phosphate, or AMP or ATP has to be uncoupled from the consumption of food in order to generate elevated blood plasma levels of adenosine without contributing to fat accumulation at the same time, as would be the case in obesity or overweight.

Therefore, in overweight or obese individuals liver ATP pools are expected to be lower than in lean individuals. This is demonstrated in a copy of an enclosed article, Nair S, Chacko VP, Arnold C and Diehl AM: Hepatic ATP Reserve and Efficiency of Replenishing: Comparison Between Obese and Nonobese Normal Individuals. The American Journal of Gastroenterology 2003, 98:466-470, which shows by direct determinations that hepatic ATP stores are inversely (negatively) correlated to the individual's body mass index (BMI) (Figure 2). The results suggest that in otherwise healthy individuals, hepatic ATP content is lower in obese individuals, compared with lean individuals, demonstrating that in obesity there is no net contribution of active agents present in food to liver ATP pools. Food however, in obese individuals contributes

directly to the individual's BMI mostly in the form of fat. In summary, the energy balance in obesity or overweight is such that the contribution of food is mostly to increased fat storage rather than to elevate liver energy stores. In obesity, fat storage is a more pronounced factor than the minute incorporation of adenosine and inorganic phosphate, AMP and ATP, which may be present in food, into hepatic ATP pools. The final result is that food consumption, in any form or diet, in obese or overweight individuals achieves the opposite result than what is suggested by the Office Action, namely an increase in hepatic ATP pools due to the adenosine and inorganic phosphate, AMP and ATP present in food.

Applicant believes that in view of the above amendment the pending application is now in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 22-0185, under Order No. 21095-00008-US1 from which the undersigned is authorized to draw.

Dated: November 29, 2007

Respectfully submitted,

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